(S119) VARIABILITY OF DOSAGE IN COMPOUNDED 4-AMINOPYRIDINE AT THREE US PHARMACIES
M. Sidovar,1 K. Hattaway,2 W. Dollard,3 R. D’Souza,4 H. Henney III1

1Medical Affairs, Acorda Therapeutics, Inc, Hawthorne, NY; 2Catalent Pharma Solutions, Research Triangle Park, NC; 3Manufacturing, Acorda Therapeutics, Inc, Hawthorne, NY; 4Technical Operations, Acorda Therapeutics, Inc, Hawthorne, NY

Background: 4-aminopyridine (4-AP) is a broad-spectrum potassium channel blocker that has been used to treat multiple sclerosis (MS) and other demyelinating conditions. The drug has been available through compounding pharmacies in different formulations, including those identified as “sustained release.” High peak plasma levels observed with immediate release (IR) formulations and compounding errors leading to overdose have been associated with serious adverse events. An extended-release tablet formulation of dalfampridine (Ampyra) was recently approved as a treatment to improve walking in patients with MS. This was demonstrated by an increase in walking speed. Dalfampridine (chemically 4-AP) was previously known as fampridine.

Objectives: This study compared analytical profiles, including dosage and dissolution, of compounded sustained-release 4-AP from three pharmacies specializing in preparing compounded products.

Methods: Capsules labeled “10 mg sustained release 4-AP” were obtained from three US pharmacies. High-performance liquid chromatography (HPLC) was used to measure potency and Level 1 content uniformity. The dissolution profile was obtained at prescribed time intervals using a USP apparatus II and HPLC. Initial testing was performed, followed by 3-month stability testing at room temperature and accelerated conditions.

Results: The uniformity of dosage between capsules was variable, ranging from 8.3 to 10.7 mg/capsule, 7.4 to 14.8 mg/capsule, and 8.6 to 11.3 mg/capsule across the three sources. Compared with Good Manufacturing Practice–manufactured extended-release dalfampridine, which completes at least 80% dissolution over 12 hours, the dissolution profile across all tested samples showed variability, with 80% to 100% of the active product released in 4 hours. These results demonstrate a dissolution profile inconsistent with an extended-release formulation.

Conclusions: The tested compounded 4-AP capsules displayed variable uniformity of dosage, with some values outside USP-accepted criteria. Although the samples were labeled as “sustained release,” their dissolution profiles more closely resembled IR characteristics. Because of the narrow therapeutic index and short half-life, using compounded drug may put patients at increased risk of adverse events and decreased duration of drug effect.

Supported by: Acorda Therapeutics